REMARKS

Applicant wishes to thank Examiner Li and Supervisor Housel for the courtesy extended to the representative, Nancy Vensko, attorney of record, on May 19, 2004. The Interview Summary Form PTOL-413 summarizes the discussions held at the personal interview. The present response to the outstanding Office Action includes the substance of the Examiner Interview.

A. Disposition of Application

Claims 2-11 and 37-39 are pending in the application. Claims 12-36 have been canceled as being drawn to non-elected subject matter. Claim 1 has been canceled, Claims 2-5 and 37 have been amended, and Claims 38 and 39 have been added to better describe the claimed invention. Thus the amendment is made for reasons unrelated to patentability. Support for the amendment is found throughout the Specification, for example, as discussed below. The Specification has been amended to include a claim to priority. An Abstract has been added to the Specification. No new matter is being added herewith.

B. Compliance with 35 USC 102/103

The Patent Office rejected Claims 1, 4-11 and 37 under 35 USC 102(a) as anticipated by Rice et al. (USP 5,874,565) in light of Doorn et al. 1995 J. Gen. Virol. 76: 1871 (see Fig. 1 on page 1873) or, in the alternative, under 35 USC 103(a) as obvious over Rice et al. (USP 5,874,565) and further in view of Yoo et al. 1995 J. Virol. 69: 32.

The Patent Office rejected Claims 1 and 4-11 under 35 USC 102(b) as anticipated by Okamoto et al. 1991 J. Gen. Virol. 72: 2697 in light of Doorn et al. 1995 J. Gen. Virol. 76: 1871 (see Fig. 1 on page 1873) or, in the alternative, under 35 USC 103(a) as obvious over Okamoto et al. 1991 J. Gen. Virol. 72: 2697 and further in view of Yoo et al. 1995 J. Virol. 69: 32.

Claims 2-3 are deemed by the Patent Office free of art. The claims must be patentable over the prior art. The references do not constitute patentability-defeating prior art.

Starting with the general state of the art, according to Yanagi et al., 1999 Virology 262: 250, at p. 250, ¶ bridging col. 1 & 2, of record, HCV is a virus that has a positive-sense single-strand RNA genome approximately 9.6 kb in length. The single long open reading frame (ORF), which encodes a polyprotein, is flanked by 5' and 3' untranslated regions (UTRs). The 5' UTR contains an

internal ribosome entry site (IRES). The 3' UTR consists of 3 regions: a short variable region, a polypyrimidine tract of variable length, and a highly conserved terminal region of approximately 100 nts. The polypyrimidine tract and the conserved region of the 3' UTR are essential for infectivity in vivo.

Turning to the references, Okamoto et al. describes the cDNA of the isolate HC-J6 but does not describe the highly conserved terminal region of approximately 100 nts essential for infectivity in vivo. Doorn et al. classifies HC-J6 as gentotype 2a (see Fig. 1 on page 1873). Rice et al. describes the highly conserved terminal region of approximately 100 nts that turns out to be essential for infectivity in vivo. Yoo et al. describes transfection of a differentiated human hepatoma cell line with in vitro-transcribed HCV RNA that lacks the polypyrimidine tract and the highly conserved terminal region of approximately 100 nts essential for infectivity in vivo (see p. 33, col. 2, "results," and FIG. 1), thus infectivity in vivo would be prevented and any perceived infectivity in vitro was probably an artifact. The references, whether taken singularly or together, neither teach nor suggest the claimed invention.

The claims are directed to a purified and isolated nucleic acid molecule which encodes human hepatitis C virus of genotype 2a, wherein the molecule encodes the amino acid sequence of SEQ ID NO: 2 or encodes an amino acid sequence that differs from that of SEQ ID NO: 2 by < 2 % at the amino acid level (structure), alternatively wherein the molecule comprises the nucleic acid sequence of SEQ ID NO: 1 or comprises a nucleic acid sequence that differs from that of SEQ ID NO: 1 by < 2% at the nucleotide level (structure), with the additional recitation that the molecule is capable of expressing said virus when transfected into cells and further capable of infectivity in vivo (function), and related DNA constructs, RNA transcripts, cells transfected thereby, and compositions thereof. According to MPEP 2163, "[t]he written description requirement for a claimed invention may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus." Here, the written description requirement is met by disclosure of relevant identifying characteristics, i.e., by a combination of such identifying characteristics (structure +

function) sufficient to show the applicant was in possession of the claimed genus.

Support for the amendment is found in the Spec. at 12: 2-7, "The present invention relates to nucleic acid sequence which comprises the genome of an infectious hepatitis C virus. More specifically, the invention relates to nucleic acid sequence which encodes infectious hepatitis C virus of strain HC-J6$_{CH}$, genotype 2a." Additional support for the amendment is found in the Spec. at Example 3, beginning on page 45, in which the infectivity of RNA transcripts was demonstrated in vivo by intrahepatic transfection of a chimpanzee. Additional support for the amendment is found in the Spec. at 39: 8-21, "Importantly, the consensus sequence of strain HC-J6$_{CH}$ (nts. 17-9629) could be determined with no ambiguity at the nucleotide or deduced amino acid level. The difference between the consensus ORF sequence of HC-J6$_{CH}$ from the experimentally infected chimpanzee and that of HC-J6 of the inoculum (Okamoto et al., 1991) was 4.1% and 2.2% at the nucleotide and deduced amino acid levels, respectively (Fig. 2, Table 2). ... Such diversities are greater than the < 2% generally considered to comprise a quasispecies." (See also Spec. at 2: 32-34.) This indicates that the consensus sequence represents a different strain of genotype 2a.

Accordingly, the pending claims properly encompass nucleic acid sequence which encodes infectious hepatitis C virus of strain HC-J6$_{CH}$. The claims are directed to a purified and isolated nucleic acid molecule which encodes human hepatitis C virus of genotype 2a, wherein the molecule encodes the amino acid sequence of SEQ ID NO: 2 (consensus sequence) or encodes an amino acid sequence that differs from that of SEQ ID NO: 2 by < 2 % at the amino acid level, alternatively wherein the molecule comprises the nucleic acid sequence of SEQ ID NO: 1 (consensus sequence) or comprises a nucleic acid sequence that differs from that of SEQ ID NO: 1 by < 2% at the nucleotide level. The scope of the claims is proper because "[t]he nucleotide and deduced amino acid sequences among isolates within a quasispecies generally differ by < 2%." Spec. at 2: 32-34.

Consequently, the claims encompassing nucleic acid sequence which encodes infectious hepatitis C virus of strain HC-J6$_{CH}$ also distinguish over HC-J6$_{OKAMOTO}$. To reiterate, the claims are directed to a purified and isolated nucleic acid molecule which encodes human hepatitis C virus of genotype 2a, wherein the molecule encodes the amino acid sequence of SEQ ID NO: 2 or encodes an amino acid sequence that differs from that of SEQ ID NO: 2 by < 2 % at the amino acid level, alternatively wherein the molecule comprises the nucleic acid sequence of SEQ ID NO: 1 or comprises a nucleic acid sequence that differs from that of SEQ ID NO: 1 by < 2% at the nucleotide

level. The claims distinguish over HC-J6$_{OKAMOTO}$ because the difference between the consensus ORF sequence of HC-J6$_{CH}$ from the experimentally infected chimpanzee and that of HC-J6 of the inoculum (Okamoto et al., 1991) was 4.1% and 2.2% at the nucleotide and deduced amino acid levels, respectively. Spec. at 39: 8-21.

For these reasons, the references, whether taken singularly or together, neither teach nor suggest the claimed invention, and thus the rejections under 35 USC 102/103 should be withdrawn.

CONCLUSION

In view of the above, it is submitted that the claims are in condition for allowance. Reconsideration and withdrawal of all outstanding rejections are respectfully requested. Allowance of the claims at an early date is solicited. If any points remain that can be resolved by telephone, the Examiner is invited to contact the undersigned at the below-given telephone number.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: 6/24/03

By: _____

Nancy W. Vensko
Registration No. 36,298
Attorney of Record
Customer No. 20,995
(805) 547-5585

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